## REMARKS

Claims 1 and 3-20 are pending in the present application.

The rejection of Claims 1, 3-4, 6-7, 11-14, and 16-17 under 35 U.S.C. §103(a) over Cavanaugh, Jr. in view of O'Connor et al is respectfully traversed.

The present invention provides, *inter alia*, a composition for the topical treatment of oropharyngeal cavity disorders, comprising an aqueous solution of the salt of diclofenac with tromethamine, wherein the amount of said salt is in an amount of 0.1% (w/w) and the pH ranges from 7 to 8. (Claim 1) The present invention also provides, *inter alia*, a composition for the topical treatment of oropharyngeal cavity disorders, comprising an aqueous solution of the salt of diclofenac with tromethamine, wherein the amount of said salt ranges from 0.1% to 0.2% (w/w) and the pH ranges from 7.6 to 8. (Claim 11) Applicants submit that none of the cited prior art can affect the patentability of the invention defined above.

Cavanaugh, Jr. is cited as providing a general disclosure of NSAIDs as well as their pH and concentrations. Column 1, lines 44-65 of Cavanaugh, Jr. is referenced by the Examiner as qualifying diclofenac as a NSAID. With respect to the pH, the Examiner points to column 5, lines 24-27 of Cavanaugh, Jr., where it is disclosed that the pH of the compositions disclosed therein can range from about 2 to about 9. In regard to the concentration of the NSAID, the Examiner points to column 5, lines 10-15 of Cavanaugh, Jr., which discloses that the concentration may generally be from about 0.02% to about 4%.

Applicants submit that it is inappropriate to consider diclofenac as a NSAID within the scope of the disclosure of Cavanaugh, Jr. as the inventors themselves do not appear to treat this compound as such. The Examiner is correct in that column 1, lines 44-65 of Cavanaugh, Jr. does state that diclofenac is a NSAID; however, diclofenac is not included in

the list of NSAIDs appearing at column 3, lines 10-19 and Claim 2. In fact, Cavanaugh, Jr. makes it quite clear that his disclosure is substantially related to ketorolac. Further, it should be noted that the only recitation of diclofenac appears at column 1, line 52.

Accordingly, Applicants submit that there is no motivation or suggestion provided by Cavanaugh, Jr. to select diclofenac as a NSAID or to apply the very generally described pH and concentrations. Moreover, even if the skilled artisan did select diclofenac, this is only the first step toward the claimed invention as the artisan would then have to substantially narrow the pH and concentration disclosed by Cavanaugh, Jr. without any guidance therein to arrive at the specifically claimed combinations of: (a) a concentration of 0.1% (w/w) at a pH ranging from 7 to 8 (see Claim 1), or (b) a concentration ranging from 0.1% to 0.2% (w/w) at a pH ranging from 7.6 to 8 (see Claim 11).

The lack of sufficient motivation to arrive at these combinations based on the disclosure of Cavanaugh, Jr. is underscored by looking at the preferred embodiments of his invention. With respect to concentration, at column 5, lines 13-14 of Cavanaugh, Jr. this reference specifically states that the most preferred concentration is from about 0.2% to about 0.8%, which is greater than the concentration in Claim 1 and only shares a common end-point with Claim 11. In regard to pH, at column 5, line 27 of Cavanaugh, Jr. this reference specifically states that the most preferred pH is from about 5 to about 6 (i.e., an acidic pH). In contrast, the pH in both Claims 1 and 11 are considerably more basic (i.e., has a higher pH).

In citing O'Connor et al, it appears that the Examiner recognizes the aforementioned deficiencies in the disclosure of Cavanaugh, Jr. Specifically, in the fourth paragraph on page 8 of the Office Action mailed March 13, 2006, the Examiner acknowledges that Cavanaugh, Jr. "does not specifically teach providing a composition having an NSID that is diclofenac in

the percent concentration and pH ranges recited in the claim[s]." The Examiner then alleges that O'Connor et al compensates for this deficiency. Applicants disagree and submit that O'Connor et al fails to compensate for the deficiency in the disclosure of Cavanaugh, Jr.

O'Connor et al disclose a salt of diclofenac and tromethamine at a pH of 7.13. Further, O'Connor et al reports that the solubility of the diclofenac/tromethamine salt is 3.95 mM, which corresponds to 0.16% (w/w). However, such a disclosure does nothing with respect to the claimed invention as O'Connor et al fails to disclose the specifically claimed combinations of concentration and pH, as follows: (a) a concentration of 0.1% (w/w) at a pH ranging from 7 to 8 (see Claim 1), or (b) a concentration ranging from 0.1% to 0.2% (w/w) at a pH ranging from 7.6 to 8 (see Claim 11).

Furthermore, Applicants submit that the present invention offers certain advantages when the specifically claimed combination of concentrations and pHs is observed. As shown in Examples 1-4, the specifically claimed combination of concentrations and pHs affords enhanced stability as compared to compositions failing meet this limitation. Applicants submit that Cavanaugh, Jr. and O'Connor et al do not offer a suggestion of this result.

Despite the foregoing, the Examiner continues to cling to the very generic teachings or concentration and pH provided by Cavanaugh, Jr., even though such a disclosure is not specifically tied to either species of compounds in the claimed invention. Specifically, the Examiner clings to the disclosure in Cavanaugh, Jr. of a pH range of 2 to 9, which embraces the claimed range of 7 to 8 (Claim 1) and 7.6 to 8 (Claim 11). The Examiner also clings to the disclosure by Cavanaugh, Jr. of a NSAID concentration of 0.02% to 4%, which embraces 0.1% (Claim 1) and the claimed range of 0.1% to 0.2% (Claim 11). It is the Examiner's position that this generic teaching in Cavanaugh, Jr. is sufficient to support a *prima facie* case of obviousness alleging that it would be obvious to vary and/or optimize the concentration

and pH to arrive at the claimed values. Apparently, it is the Examiner's position that Cavanaugh, Jr. would support this rejection despite the fact that the claimed invention is effectively four-steps removed from Cavanaugh, Jr.: (1) selection of diclofenac as a NSAID despite the lack of a specific disclosure to this effect, (2) selection of the specific concentration, despite the lack of a specific disclosure of this range, (3) selection of the specific pH range, despite the lack of a specific disclosure of this range, and (4) putting the selected concentration and pH together to arrive a the specifically claimed relationship. Again, Applicants submit that there is insufficient motivation provided by Cavanaugh, Jr. even when viewed together with O'Connor et al to arrive at this conclusion.

Accordingly, the combined disclosures of Cavanaugh, Jr. and O'Connor et al fail to specifically direct the artisan to make the four required steps from the disclosure of Cavanaugh, Jr. to the invention as claimed. First, the artisan would have to select diclofenac as a NSAID. Second, the artisan would have to select the specifically claimed concentration or concentration range. Third, the artisan would have to select the specifically claimed pH ranges. Fourth, the artisan would have to properly combine the selected concentration and the pH per the specifically claimed invention. Applicants submit that there is absolutely nothing in the disclosures of Cavanaugh, Jr. and O'Connor et al to direct such a selection process.

Applicants kindly ask that the Office not use their disclosure as a guidepost to piece together their invention from the deficient disclosures of Cavanaugh, Jr. and O'Connor et al. The question that the Examiner should ask is why, absent Applicants' disclosure, would the artisan be motivated to arrive at the present invention when neither Cavanaugh, Jr. nor O'Connor et al sufficiently specify that which Applicants have invented? O'Connor et al in hand, the skilled artisan would have no reasonable expectation of the advantages flowing

from the claimed invention. To illustrate the superior effects provided by the present invention, Applicants **submit herewith** a Declaration under 37 C.F.R. §1.132 executed by Dr. Mario Pinza ("the Pinza Declaration"). In the Pinza Declaration, two different oral rinse preparations (preparations A and B), representative of the combined disclosures of Cavanaugh, Jr. and O'Connor et al, were prepared in which diclofenac tromethamine was present at 0.104 %(w/w), which due to rounding and significant figure would be within the scope of the claimed 0.1 %(w/w) of Claim 1 and the range of 0.1 to 0.2 %(w/w) of Claim 11, and the pH was 6.8. These Oral Rinse preparations proved to be unstable with formulation A exhibiting a small amount of precipitate after 10 days at room temperature and formulation B exhibiting a small amount of precipitate after 15 days at room temperature (see paragraph 6 of the Pinza Declaration). In contrast, when the pH of oral rinse preparations A and B was raised to 7.8 (preparations C and D, respectively), a stable formulation is prepared without any precipitate after six months of accelerated stability (see paragraph 6 of the Pinza Declaration).

In view of this discovery, in paragraph 6 of the Pinza Declaration Dr. Pinze concludes: "This behaviour was entirely unexpected as regards the mouthwashes containing an amount of salt of diclofenac with tromethamine that is less than the solubility limit reported by Fini et al. (cited above). Further, these data clearly demonstrate the criticality of the pH range of 7 to 8 as compared to the pH range of 2 to 9 which is disclosed in Cavanaugh Jr. (U.S. 5,626,838) for NSAIDs, including diclofenac. In fact, from the disclosure of Cavanaugh Jr. the skilled artisan would expect that the operating pH range of NSAIDs would be acidic (see column 5, lines 24-27 which indicates that the preferred pH is from about 4 to about 7, more preferably from about 5 to about 6). Clearly the foregoing data demonstrates that, unexpectedly, the stability advantage of the present invention is only obtained when the pH

ranges from 7 to 8 rather than acidic as approximated by oral rinse formulations A and B (pH 6.8)."

In view of the foregoing, Applicants submit that the presently claimed invention is not obvious over the combined disclosures of Cavanaugh, Jr. and O'Connor et al. Further, Applicants submit that the Pinza Declaration should rebut even the alleged *prima facie* case of obviousness.

Therefore, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 5 and 15 under 35 U.S.C. §103(a) over Cavanaugh, Jr. in view of O'Connor et al and Bianchi et al is respectfully traversed.

Cavanaugh, Jr. and O'Connor et al have been discussed above in relation to independent Claims 1 and 11. Bianchi et al is cited for its disclosure of an aqueous-based dentifrice composition containing a polyoxyethylene polyoxypropylene block copolymer. However, Applicants submit that Bianchi et al fails to compensate for the aforementioned deficiencies in the combined disclosures of Cavanaugh, Jr. and O'Connor et al. Accordingly, the combined disclosures of Cavanaugh, Jr., O'Connor et al, and Bianchi et al fails to render the present invention obvious.

Applicants request withdrawal of this ground of rejection.

In the Office Action, the Examiner alleges that Claims 8-10 and 18-20 are directed to an invention that is independent or distinct from the invention originally claimed. However, this assertion is not entirely correct. Claims 8-10 and 18-20 depend directly from the invention originally claimed.

Further, the Examiner has characterized the relationship between the originally presented claims and pending Claims 8-10 and 18-20 as a product and a process of use. Citing MPEP §806.05(h), the Office suggests that the "product as claimed can be used in a materially different process of using the product, such as in the treatment of other inflammatory disorders treatable by orally administered NSAIDs." However, the Office has not provided sufficient reasons and/or examples to support this assertion. The Office has merely stated the conclusion. Accordingly, the Office has failed to meet the burden necessary in order to sustain the Restriction Requirement. Accordingly, Applicants respectfully submit that the Restriction Requirement should be withdrawn.

Moreover, the MPEP in §803 states as follows:

> "If the search and examination of an entire application can be made without a serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions."

Applicants respectfully submit that a search of all the claims would not impose a serious burden on the Office.

Finally, Applicants remind the Examiner of MPEP §821.04

> ...if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Upon a finding of allowability of the elected product claims, Applicants respectfully request rejoinder of withdrawn process claims.

Applicants submit that the present application is now in condition for allowance.

Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Vincent K. Shier, Ph.D.
Registration No. 50,552

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/03)